AD_____

Award Number: DAMD17-98-1-8238

TITLE: Post-Mastectomy and Phantom Breast Pain: Risk Factors, Natural History, and Impact on Quality of Life

PRINCIPAL INVESTIGATOR: Robert Dworkin, Ph.D.

CONTRACTING ORGANIZATION: The University of Rochester
Rochester, New York 14627

REPORT DATE: July 2001

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 2001	Annual (1 Jul 00 - 30 Jun 01)

4. TITLE AND SUBTITLE
Post-Mastectomy and Phantom Breast Pain: Risk Factors, Natural History, and Impact on Quality of Life

5. FUNDING NUMBERS
DAMD17-98-1-8238

6. AUTHOR(S)
Robert Dworkin, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Rochester
Rochester, New York 14627

E-Mail: robert_dworkin@urmc.rochester.edu

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
Report contains color

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

Post-mastectomy pain syndrome (PMPS), phantom breast pain, and post-lumpectomy pain are poorly understood chronic pain syndromes that occur following surgical procedures for breast cancer. These pain syndromes are not well studied, but there is appreciable evidence that patients can be significantly disabled by their chronic pain and can suffer from substantial reductions in quality of life. The primary aims of this research project are to identify risk factors for chronic pain following surgical procedures for breast cancer, characterize its natural history, and examine its impact on quality of life using a prospective research design. To date, 103 women scheduled for breast cancer surgery have been assessed with respect to hypothesized risk factors for chronic pain. These women are studied for one year following their surgery, with periodic assessments of pain, health-related quality of life, and psychosocial variables. This allows risk factors for chronic pain to be identified and its impact on quality of life to be determined. The pathogenesis of chronic pain following breast cancer surgery is unknown, and the identification of risk factors constitutes an important first step in understanding the processes by which chronic pain develops; this knowledge may lead to the development of more effective treatment approaches. By identifying risk factors, the results can also be used to design interventions aimed at preventing the development of chronic pain following surgical procedures for breast cancer. Moreover, the identification of risk factors will make it possible to determine which patients are most in need of such preventive efforts.

14. SUBJECT TERMS
breast cancer, chronic pain, mastectomy, lumpectomy, post-mastectomy, pain syndrome

15. NUMBER OF PAGES
19

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Cover..... 1

SF 298..... 2

Table of Contents..... 3

Introduction..... 4

Body..... 4

Key Research Accomplishments..... 10

Reportable Outcomes..... 10

Conclusions..... 10

References..... 11

Appendices..... 14

Introduction

Post-mastectomy pain syndrome (PMPS), post-lumpectomy pain, and phantom breast pain are poorly understood chronic pain syndromes that occur following surgical procedures for breast cancer. The primary aims of this research are to identify risk factors for these chronic pain syndromes following surgical procedures for breast cancer, characterize their natural history, and examine their impact on quality of life using a prospective research design. Women scheduled for mastectomy, lumpectomy, or excisional biopsy are being assessed with respect to hypothesized risk factors for chronic pain and are then being studied prospectively for one year. Periodic follow-up assessments of pain, health-related disability and quality of life, and selected psychosocial variables will allow risk factors to be identified and the impact of chronic pain on quality of life to be determined. An important feature of this research is its detailed assessment of pre-operative, early post-operative, and chronic pain; in these assessments, sensory and affective aspects of pain, pain quality, and non-painful abnormal sensations are being examined. By identifying risk factors for chronic pain following surgical procedures for breast cancer, the results of this research can be used to design interventions aimed at preventing the development of these chronic pain syndromes.

Body of Annual Report

Chronic pain has been defined as pain that persists beyond the normal time of healing, a definition which includes most painful conditions that have lasted longer than three months (Merskey & Bogduk, 1994). Chronic pain is both a medical and a behavioral problem and it is accompanied by substantial economic costs to society as well as great personal suffering. The current research is a prospective study of the development of post-mastectomy pain syndrome (PMPS), post-lumpectomy pain, and phantom breast pain. Current understanding of these chronic pain syndromes is limited, and of these different types of chronic pain following breast cancer surgery, post-lumpectomy pain has been the least well studied. It has been suggested that PMPS is caused by surgical injury to the intercostobrachial nerve (Foley, 1987; Vecht et al., 1989; Stevens et al., 1995; cf. Watson et al., 1989, who noted that in some patients the cutaneous branches of other intercostal nerves are also involved). The pathophysiology of phantom breast pain—as well as other phantom pains—remains obscure (Katz & Melzack, 1990; Melzack, 1990, 1996; Sherman, 1997). In a recent review, most reports of the prevalence of PMPS were within the range of 16% to approximately 50% (Kwekkeboom, 1996). Not included in this review were two recent studies of PMPS in which 39% of 181 patients reported pain at least one year after surgery (Wallace et al., 1996) and 20% of 95 patients reported "chronic, stable pain of long duration" beginning within days to weeks after surgery (Stevens et al., 1995, p. 63). Early studies of phantom breast pain (excluding non-painful phantom breast sensations) reported prevalences ranging from 18-54% (Jamison et al., 1979), and a recent study found phantom breast pain present in 13% of patients three weeks and one year after mastectomy and in 17% of patients at six years (Krøner, 1989, 1992). Although the prevalence of PMPS and phantom breast pain might be expected to decrease with duration of time since surgery, the results of several studies indicate that this may not occur (Krøner et al., 1989, 1992; Vecht et al., 1989; Maunsell et al., 1993). It has been suggested that women are often reluctant to report pain following mastectomy to their physicians, which may contribute not only to the impression that pain following mastectomy is rare but also to the variability in the results of studies of the prevalence of PMPS and phantom breast pain

(Jamison et al., 1979, Abraham & Llewellyn-Jones, 1983; Staps et al., 1985). Importantly, both PMPS and phantom breast pain have been found to have a significant negative impact on psychological adjustment, the performance of daily occupational and domestic activities, and quality of life (e.g., Jamison et al., 1979; Christensen et al., 1982; Hladiuk et al., 1992; Maunsell et al., 1993; Stevens et al., 1995).

Very few studies have examined risk factors for pain following mastectomy, and no consistent relationships have emerged between the likelihood of persisting pain and age, type of mastectomy, cancer treatment, or post-operative sequelae (Jamison et al., 1979; Christensen et al., 1982; Krøner et al., 1989, 1992). In one recent study, women with pre-mastectomy breast pain were more likely to have phantom breast pain three weeks, one year, and six years after surgery than those without pre-mastectomy pain (Krøner et al., 1989, 1992). The results of studies of limb amputees are consistent with this finding (Jensen et al., 1985; Katz & Melzack, 1990; Weiss & Lindell, 1996). The results of these studies suggest that patients with pain before either a mastectomy or a limb amputation are at greater risk for the development of phantom pain. Moreover, the risk appears greatest for patients with more severe pain, and it has been hypothesized that phantom pain may develop when the combination of pre-amputation pain intensity and duration exceeds a critical threshold (Katz & Melzack, 1990).

The presence of psychosocial distress in patients with pain following mastectomy has been interpreted as evidence that psychosocial factors contribute to the development of pain (Woods, 1975; Jamison et al., 1979; Christensen et al., 1982). However, psychosocial distress can be a consequence of living with prolonged pain, and the absence of prospective studies has made it impossible to determine whether psychological abnormalities in patients following mastectomy and limb amputation are risk factors that preceded the development of chronic pain or are consequences of it (Sherman et al., 1987; Katz, 1992). Nevertheless, there is evidence that stress can precede increases in phantom pain (Arena et al., 1990), and the results of prospective studies suggest that psychosocial factors can be risk factors for other pain syndromes (Dworkin, 1997a) as well as for pain associated with cancer treatment (Syrjala & Chapko, 1995). It is therefore important to determine whether patients who have greater psychosocial distress before surgical procedures for breast cancer are more likely to develop chronic pain.

The theoretical approach on which this research is based is one in which the development of chronic pain is considered the result of an interaction between biological and psychosocial processes. The principal investigator and his colleagues have proposed that the results of chronic pain research are consistent with a diathesis-stress model (e.g., Dworkin & Portenoy, 1996; Dworkin & Banks, 1999). In this approach, an interaction between an organic condition (the diathesis) and various psychosocial factors (the stress component of the model) is hypothesized to account for the development of chronic pain. The diathesis-stress approach provides a heuristic model that can be used in the design of research on the development of chronic pain following breast cancer surgery. In such a model, a mastectomy or lumpectomy and the nerve damage associated with these procedures can be considered the diathesis for chronic pain; various psychosocial factors constitute the stress (broadly defined) that results in a process whereby acute peri-operative pain becomes the chronic pain of PMPS, post-lumpectomy pain, or phantom breast pain.

The prospective study of mastectomy and lumpectomy patients has the potential to identify risk factors derived from this model for the development of chronic pain following surgical procedures for breast cancer. To identify risk factors, patients with pain at a 3-month follow-up interview are considered to have chronic pain (Merskey & Bogduk, 1994). Patients who do and do not develop chronic pain will be compared with respect to each of the measures in five families of variables assessed pre-operatively—demographic and medical/surgical, acute pain, health-related disability, psychological distress, and social support and life events. Because the results of cross-sectional studies that have attempted to identify risk factors for chronic pain following breast cancer surgery within the demographic and medical/surgical domain have been inconsistent, it is hypothesized that there will be no significant risk factors within these families of variables. As reviewed in Dworkin (1997a), the results of a number of studies indicate that more severe acute pain and greater psychosocial distress are risk factors for the development of chronic pain. It is therefore hypothesized that acute pain intensity and duration and measures within the two families of psychosocial variables will be significant risk factors for PMPS, post-lumpectomy pain, and phantom breast pain.

A second aim of this research is to examine the psychosocial consequences of chronic pain following surgical procedures for breast cancer. It has been proposed that the assessment of chronic pain patients should be multidimensional (Turk & Rudy, 1987; Dworkin, 1997b). This approach has been used as a basis for selecting measures of the impact of chronic pain on psychological distress and quality of life. It is hypothesized that psychological distress, maladaptive illness beliefs, and health-related physical, role, and social disability will increase in patients with persisting chronic pain from the 3-month follow up through the final follow-up assessment at 12 months.

Methods

English-speaking women 18 years of age and older scheduled for mastectomy, lumpectomy, or excisional biopsy are being recruited from the surgical service at Strong Memorial Hospital (SMH). The inclusion of patients scheduled for lumpectomy and excisional biopsy represents a modification to the original research protocol. This change was made based on the increasing reliance of surgeons on these more conservative surgical procedures for the treatment of early stage breast cancer. Approval for this modification was obtained from the U.S. Army Medical Research and Materiel Command and from the University of Rochester Research Subjects Review Board.

Women scheduled for breast surgery at SMH whose names and telephone numbers are released by their attending surgeon are being contacted and the study is described to them over the telephone. Those who agree to participate have their pre-operative assessment scheduled within two weeks of their surgery. At this assessment, the patient is asked to sign an informed consent form. A project coordinator conducts subject recruitment and the pre-operative assessments. Most of these assessments are conducted in patients' homes to facilitate their participation. Some assessments are conducted at SMH, if the patient so desires or if it is deemed unsafe for the research personnel to visit the patient's home. Patients are reimbursed $80 for participation in the research in two installments—$40 at the conclusion of the pre-operative assessment, and $40 upon completion of the 12-month follow-up interview. To date, 104 women have been enrolled in the research, have had their pre-operative assessment, and are undergoing follow-up assessments. This constitutes

successful progress with respect to the accomplishment of Tasks 1, 2, 5, and 6 in the approved Statement of Work.

Post-operative pain and analgesic use are being assessed in hospital visits or telephone interviews at 2 and 10 days after surgery; this will make it possible to examine the relationships between acute post-operative pain and analgesic equivalence levels (Steedman et al., 1992) and the development of chronic pain. At 1, 3, 7, and 12 months following surgery, telephone interviews are being conducted in which surgery-related pain and disability, analgesic use, health status and treatment history since the previous assessment are assessed. Surgery-related pain at the 3, 7, and 12 month follow-up interviews will be considered chronic pain (Merskey & Bogduk, 1994). The criteria of Watson et al. (1992) will be used to diagnose PMPS and the criteria of Krøner et al. (1989, 1992) will be used to diagnose phantom breast sensations and phantom breast pain. Use of these criteria will ensure that PMPS and phantom breast pain are distinguished from other types of pain that may be present at these follow-up interviews, including radiation plexopathy and neuritis (e.g., Watson & Evans, 1982; Watson et al., 1989) and post-mastectomy scar pain (e.g., Krøner et al., 1989, 1992).

To examine whether persisting pain is accompanied by increasing psychosocial distress, the questionnaire measures of depression, anxiety, disease conviction, and somatization are also administered during the follow-up interviews. These interviews are conducted by a member of the research team who did not conduct the initial assessments, who is therefore blind with respect to the patient's pre-operative psychological status. Because the identities of patients who do and do not develop pain will only become known at the follow-up interviews, the project coordinator conducting the pre-operative assessments will be blind with respect to the data used to identify risk factors for chronic pain.

Measures

Demographic and medical/surgical measures. Basic demographic data—age, race, marital status, number of children, living arrangements, years of education, occupation, and current employment status—are assessed at the beginning of the pre-operative assessment. The subject's medical history is assessed by means of an expanded version of the physical health section of the Life Stressors and Social Resources Inventory (see below; Moos & Moos, 1994). Information regarding past and current illnesses and treatments, including past and current painful conditions (based on the methods of S.F. Dworkin et al., 1990), is obtained from this interview.

Information regarding the patient's breast cancer history, type of surgery, and degree of sparing of the intercostobrachial nerve is obtained from the attending surgeon and operative report. The type and duration of operative and post-operative anesthesia and analgesia is recorded from the patient's hospital records, and information regarding the dosage and portal of entry of any radiation treatment following surgery is obtained from the patient's radiation oncologist. At the present time, collection of this information on the subjects who have completed the study or who are presently enrolled in the research is ongoing (Tasks 3 and 4 in the approved Statement of Work).

Pre-operative pain, early post-operative pain, and chronic pain. Comprehensive assessments of pre-operative pain, early post-operative pain, PMPS, post-lumpectomy chronic pain, and phantom

breast pain are being conducted using the Brief Pain Inventory Short-form (BPI; Cleeland & Syrjala, 1992) and the McGill Pain Questionnaire (MPQ; Melzack, 1975); the reliability and validity of both measures has been extensively documented. The BPI was developed specifically for use in assessing cancer pain, and the MPQ provides an assessment of both sensory and affective aspects of pain, as well as providing a characterization of pain quality. No previous studies of chronic pain following breast cancer surgery have distinguished the sensory and affective aspects of pain, a central component of current pain research (e.g., Fernandez & Turk, 1992; Chapman, 1993), nor have pain quality and abnormal but non-painful sensations in these syndromes been carefully assessed. Indeed, in some studes of phantom breast pain, painful and non-painful phantom breast sensations have not been clearly distinguished (e.g., Christensen et al., 1982; Karydas et al., 1986).

Many amputees describe phantom limb pain "as indistinguishable from the pain they experienced in the limb prior to amputation" (Katz, 1992, p. 282), and the MPQ will also be used to examine the hypothesis that the quality of any pre-mastectomy pain and the quality of PMPS and phantom breast pain are similar. In addition, administering the MPQ will make it possible to examine whether the predominant qualities of phantom breast pain remain the same in the year following surgery, as has been reported by Krøner et al. (1989).

Health-related disability, quality of life, and psychological distress. At the pre-operative assessment, patients are administered the Medical Outcomes Study short-form health survey (SF-36; Ware et al., 1992) as well as the Functional Assessment of Cancer Therapy-Breast (FACT-B; Brady et al, 1997). The SF-36 will provide measures of health-related physical, role, and social disability in the week immediately prior to surgery. The impact of post-surgical pain on quality of life at each of the follow-up interviews is assessed by readministering the FACT-B at the 1, 3, 7 and 12 month follow-up assessments.

Depression and anxiety have been found to be risk factors for chronic pain as well as consequences of chronic pain (Banks & Kerns, 1996; Dworkin, 1997a), and measures of both are administered at the pre-operative assessment and at the 1, 3, 7, and 12 month follow-up interviews. The Hamilton rating scales for depression and anxiety (Hamilton, 1959, 1960) are administered at the pre-operative assessment using structured interviews developed for these measures (Williams, 1988, unpublished manual). To complement these interview-based assessments, two self-report measures of symptoms of depression and anxiety are also administered—the Beck Depression Inventory (Beck et al., 1961), a measure of depression that has been used in a large number of studies of chronic pain, and the State-Trait Anxiety Inventory, state version (Spielberger, 1977), a measure of the extent to which an individual feels anxious at the time of testing. The combined use of these interviews and questionnaires provides an assessment of the moderately severe forms of depression and anxiety that appear to be both risk factors for and consequences of chronic pain.

Several measures that reflect the individual's beliefs about physical illness and somatic symptoms are also administered at both the pre-operative assessment and at the 1, 3, 7, and 12 month follow-up interviews. These are the Illness Behavior Questionnaire disease conviction scale (Pilowsky, 1989), the Somatosensory Amplification Scale (Barsky et al., 1990), and the Somatic Symptom Inventory (Barsky et al., 1990). As reviewed in Dworkin et al. (1996), these measures have been reported to have important relationships with chronic pain in both cross-sectional and prospective studies. Their

administration will make it possible to evaluate whether maladaptive beliefs about relationships between physical symptoms and illness and heightened awareness of physical symptoms are risk factors for or consequences of pain following mastectomy.

Social support and life events. Moos (1992) has argued that social supports and life events are closely interrelated and influence each other over time, and that an integrated approach to their assessment is therefore necessary. It has also been noted that whereas most existing measures of life events have focused on temporally discrete events, many psychological and physical disorders may be more closely associated with ongoing chronic stressors (e.g., Monroe & Roberts, 1990; Moos, 1992). Based on these considerations, Moos and his colleagues (Moos, 1992; Moos & Moos, 1994) developed a measure—the Life Stressors and Social Resources Inventory (LISRES)—that has been used in a variety of populations to provide an integrated assessment of chronic stressors, discrete life events, and social supports. The LISRES is administered at the pre-operative assessment to test the hypothesis that decreased social support and stressful life events are risk factors for the development of PMPS and phantom breast pain following mastectomy.

Key Research Accomplishments

1. 104 patients have been enrolled and are currently actively participating in the research protocol.

2. Two participants have withdrawn from participation in the study; four participants changed residences or telephone numbers and could not be contacted for follow-up.

3. Computer-scannable data collection forms have been prepared to ensure accurate data entry and minimize the amount of effort required for data verification.

4. These accomplishments constitute successful progress with respect to Tasks 1, 2, 5, 6, and 7 described in the approved Statement of Work.

Reportable Outcomes

Dworkin, R.H., Kulick, D.I., Andrus, C.H., Hogan, L.H., Nagasako, E.M., Pennella-Vaughan, J., and Perkins, F.M. Chronic pain following breast cancer surgery. Paper presented at the Department of Defense Breast Cancer Research Program Era of Hope meeting, Atlanta, Georgia, June 2000.

Kulick, D.I., Hogan, L.H., Nagasako, E.M., Andrus, C.H., and Dworkin, R.H. Chronic pain following breast cancer surgery: Prevalence and risk factors. Paper presented at the 21st annual scientific meeting of the American Pain Society, Phoenix, Arizona, April 2001.

Dworkin, R.H., Nagasako, E.M., and Galer, B.S. (2001). Assessment of neuropathic pain. In D.C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (2nd ed.). New York: Guilford Press.

Conclusions

Recruitment of subjects and collection of data are ongoing and interim analyses of the data have been conducted. The results of these analyses suggest that age, presence of malignancy, presence of pre-operative pain and early post-operative acute pain, higher pre-operative anxiety, and greater illness concern may be risk factors for the development of chronic pain following surgical procedures for breast cancer. These risk factors and additional variables will be re-examined when the sample is fully enrolled (n=200), at which time additional risk factors may also be identified.

Identification of risk factors for chronic pain following breast surgery will enhance understanding of the processes by which such pain develops and may lead to the development of more effective preventive interventions and treatment approaches.

References

Abraham, S.F., Llewellyn-Jones, D. (1983). Phantom breast sensation. *Medical Journal of Australia,* 1:9.

Arena, J.G., Sherman, R.A., Bruno, G.M., Smith, J.D. (1990). The relationship between situational stress and phantom limb pain: Cross-lagged correlational data from six month pain logs. *Journal of Psychosomatic Research,* 34:71-77.

Banks, S.M., Kerns, R.D. (1996). Explaining high rates of depression in chronic pain: A diathesis-stress framework. *Psychological Bulletin,* 119:95-110.

Barsky, A.J., Wyshak, G., Klerman, G.L. (1990). The somatosensory amplification scale and its relationship to hypochondriasis. *Journal of Psychiatric Research,* 24:323-334.

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry,* 4:561-571.

Brady, M.J., Cella, D.F., Mo, F., Bonomi, A.E., Tulsky, D.S., Lloyd, S.R., Deasy, S., Cobleigh, M., & Shiomoto, G. (1997). Reliability and validity of the Functional Assessment of Cancer Therapy-Breast (FACT-B) quality of life instrument. *Journal of Clinical Oncology,* 15, 974-986.

Bray, J.H., Maxwell, S.E. (1985). *Multivariate analysis of variance.* Newbury Park, CA: Sage.

Chapman, C.R. (1993). The emotional aspects of pain. In C.R. Chapman, K.M. Foley (Eds.), *Current and emerging issues in cancer pain: Research and practice.* New York: Raven.

Christensen, K., Blichert-Toft, M., Giersing, U., Richardt, C., Beckmann, J. (1982). Phantom breast syndrome in young women after mastectomy for breast cancer. *Acta Chirurgica Scandinavica,* 148:351-354.

Cleeland, C.S., Syrjala, K.L. (1992). How to assess cancer pain. In D.C. Turk, R. Melzack (Eds.), *Handbook of pain assessment.* New York: Guilford.

Dworkin, R.H. (1997a). Which individuals with acute pain are most likely to develop a chronic pain syndrome? *Pain Forum,* 6:127-136.

Dworkin, R.H. (1997b). Toward a clearer specification of acute pain risk factors and chronic pain outcomes. *Pain Forum,* 6:148-150.

Dworkin, R.H., Banks, S.M. (1999). A vulnerability-diathesis-stress model of chronic pain: Herpes zoster and the development of postherpetic neuralgia. In R.J. Gatchel, D.C. Turk (Eds.), *Psychosocial factors in pain: Critical perspectives.* New York: Guilford.

Dworkin, R.H., Cooper, E.M., Siegfried, R.N. (1996). Chronic pain and disease conviction. *Clinical Journal of Pain,* 12:111-117.

Dworkin, R.H., Portenoy, R.K. (1996). Pain and its persistence in herpes zoster. *Pain,* 67:241-251.

Dworkin, S.F., Von Korff, M., LeResche, L. (1990). Multiple pains and psychiatric disturbance: An epidemiologic investigation. *Archives of General Psychiatry,* 47:239-244.

Fernandez, E., Turk, D.C. (1992). Sensory and affective components of pain: Separation and synthesis. *Psychological Bulletin,* 112:205-217.

Foley, K.M. (1987). Pain syndromes in patients with cancer. *Medical Clinics of North America,* 71:169-184.

Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology,* 32:50-55.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry,* 23:56-62.

Hladiuk, M., Huchcroft, S., Temple, W., Schnurr, B.E. (1992). Arm function after axillary dissection for breast cancer: A pilot study to provide parameter estimates. *Journal of Surgical Oncology,* 50:47-52.

Jamison, K., Wellisch, D.K., Katz, R.L., Pasnau, R.O. (1979). Phantom breast syndrome. *Archives of Surgery,* 114:93-95.

Jensen, T.S., Krebs, B., Nielsen, J., Rasmussen, P. (1985). Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain,* 21:267-278.

Karydas, I., Fentiman, I.S., Habib, F., Hayward, J.L. (1986). Sensory changes after treatment of operable breast cancer. *Breast Cancer Research & Treatment,* 8:55-59.

Katz, J. (1992). Psychophysiological contributions to phantom limbs. *Canadian Journal of Psychiatry,* 37:282-298.

Katz, J., Melzack, R. (1990). Pain 'memories' in phantom limbs: Review and clinical observations. *Pain,* 43:319-336.

Krøner, K., Knudsen, U.B., Lundby, L., Hvid, H. (1992). Long-term phantom breast syndrome after mastectomy. *Clinical Journal of Pain,* 8:346-350.

Krøner, K., Krebs, B., Skov, J., Jørgensen, H.S. (1989). Immediate and long-term phantom breast syndrome after mastectomy: Incidence, clinical characteristics and relationship to pre-mastectomy breast pain. *Pain,* 36:327-334.

Kwekkeboom, K. (1996). Postmastectomy pain syndromes. *Cancer Nursing,* 19:37-43.

Maunsell, E., Brisson, J., Deschênes, L. (1993). Arm problems and psychological distress after surgery for breast cancer. *Canadian Journal of Surgery,* 36:315-320.

Melzack, R. (1975). The McGill pain questionnaire: Major properties and scoring methods. *Pain,* 1:277-299.

Melzack, R. (1990). Phantom limbs and the concept of a neuromatrix. *Trends in Neurosciences,* 13:88-92.

Melzack, R. (1996). Gate control theory: On the evolution of pain concepts. *Pain Forum,* 5:128-138.

Merskey, H., Bogduk, N. (Eds.). (1986). *Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms* (2nd ed.). Seattle, WA: IASP Press.

Monroe, S.M., Roberts, J.E. (1990). Conceptualizing and measuring life stress: Problems, principles, procedures, progress. *Stress Medicine,* 6:209-216.

Moos, R.H. (1992). Understanding individuals' life contexts: Implications for stress reduction and prevention. In M. Kessler, S.E. Goldston, J.M. Joffe (Eds.), *The present and future of prevention.* Newbury Park, CA: Sage.

Moos, R.H., Moos, B.S. (1994). *Life stressors and social resources inventory—adult form (LISRES-A): Professional manual.* Odessa, FL: Psychological Assessment Resources.

Pilowsky, I. (1989). Pain and illness behaviour: Assessment and management. In P.D. Wall, R. Melzack (Eds.), *Textbook of pain (2nd ed.).* Edinburgh: Churchill Livingstone.

Sherman, R.A. (Ed.). (1997). *Phantom pain.* New York: Plenum

Sherman, R.A., Sherman, C.J., Bruno, G.M. (1987). Psychological factors influencing chronic phantom limb pain: An analysis of the literature. *Pain,* 28:285-295.

Spielberger, C.D. (1977). *State-trait anxiety inventory.* Palo Alto: Consulting Psychologists Press.

Staps, T., Hoogenhout, J., Wobbes, T. (1985). Phantom breast sensations following mastectomy. *Cancer,* 56:2898-2901.

Steedman, S.M., Middaugh, S.J., Kee, W.G., Carson, D.S., Harden, R.N., Miller, M.C. (1992). Chronic pain medications: Equivalence levels and method of quantifying drug usage. *Clinical Journal of Pain,* 8:204-214.

Stevens, P.E., Dibble, S.L., Miaskowski, C. (1995). Prevalence, characteristics, and impact of postmastectomy pain syndrome: An investigation of women's experiences. *Pain,* 61:61-68.

Syrjala, K.L., Chapko, M.E. (1995). Evidence for a biopsychosocial model of cancer treatment-related pain. *Pain,* 61:69-79.

Turk, D.C., Rudy, T.E. (1987). Towards a comprehensive assessment of chronic pain patients. *Behavior Research and Therapy,* 25:237-249.

Vecht, C.J., Van de Brand, H.J., Wajer, O.J.M. (1989). Post-axillary dissection pain in breast cancer due to a lesion of the intercostobrachial nerve. *Pain,* 38:171-176.

Wallace, M.S., Wallace, A.M., Lee, J., Dobke, M.K. (1996). Pain after breast surgery: A survey of 282 women. *Pain,* 66:195-205.

Ware, J.E., Sherbourne, C.D. (1992). The MOS 36-item short-form health survey (SF-36): Conceptual framework and item selection. *Medical Care,* 30:473-483.

Watson, C.P.N., Evans, R.J. (1982). Intractable pain with breast cancer. *Canadian Medical Association Journal,* 126:263-266.

Watson, C.P.N., Evans, R.J. (1992). The postmastectomy pain syndrome and topical capsaicin: A randomized trial. *Pain,* 51:375-379.

Watson, C.P.N., Evans, R.J., Watt, V.R. (1989). The post-mastectomy pain syndrome and the effect of topical capsaicin. *Pain,* 38:177-186.

Weiss, S.A., Lindell, B. (1996). Phantom limb pain and etiology of amputation in unilateral lower extremity amputees. *Journal of Pain and Symptom Management,* 11:3-17.

Williams, J.B.W. (1988). A structured interview guide for the Hamilton Depression Rating Scale. *Archives of General Psychiatry,* 45:742-747.

Woods, N.F. (1975). Psychologic aspects of breast cancer: Review of the literature. *Journal of Obstetric, Gynecologic, and Neonatal Nursing,* 4:15-22.

Chronic Pain Following Breast Cancer Surgery

R.H. Dworkin, D.I. Kulick, C.H. Andrus, L.H. Hogan,
E.M. Nagasako, J. Pennella-Vaughan and F.M. Perkins

Departments of Anesthesiology and Surgery
University of Rochester Medical Center, Rochester, New York

Presented at the Department of Defense Research Program Meeting
Era of Hope, Atlanta, Georgia, June, 2000

Introduction

As many as 55% of women who undergo surgery for breast cancer develop post-surgical pain that may persist for months to years[1]. Although little is known about such pain syndromes once they have become chronic (i.e., at least three months following surgery), it is clear that patients can be significantly disabled and may experience substantial reductions in quality of life. The primary aims of this study are to identify risk factors for chronic pain following surgery for breast cancer, characterize its natural history, and examine its impact on women's quality of life.

Methods

Subjects

- 54 patients who have undergone breast surgery for cancer (200 anticipated by conclusion of study)
- English-speaking and at least age 18
- Recruited from surgical service at Strong Memorial Hospital, Rochester, NY

Procedures

- Women scheduled for breast surgery for cancer who authorized the release of their names and telephone numbers to the study coordinator were contacted to describe the nature of the study and determine interest in participation.
- Those who agreed to participate were interviewed pre-operatively, within two weeks of surgery.
- A variety of interview and questionnaire measures of demographic, medical, pain, and psychosocial status were administered at this initial assessment.
- Post-operative pain and analgesic use were assessed via telephone interviews at 2 and 10 days after surgery.
- At 1, 3, 7, and 12 months following surgery, telephone interviews were conducted in which persisting surgery-related pain and disability, analgesic use, interim health status and treatment history, and psychological distress were assessed.
- The individuals conducting these follow-up interviews were blind with respect to the information collected during the initial assessment.

Measures: Initial assessment

- The present analyses are focused on comparing patients who did and did not report some degree of persisting pain at three months after surgery with respect to measures administered at the initial assessment.
- Age, presence of pre-operative breast pain, presence of malignancy, history of diagnostic core biopsy, type of surgery, acute post-operative pain, and four sets of psychosocial measures hypothesized to predict chronic pain were examined:
  1. Depression: Hamilton Rating Scales - Depression (HAM-D)[2] and Beck Depression Inventory (BDI)[3]
  2. State anxiety: State-Trait Anxiety Inventory, state version (STAI)[4]
  3. Disease conviction: Illness Behavior Questionnaire disease conviction scale (IBQ)[5]
  4. Somatosensory focus: Somatosensory Amplification Scale (SAS)[6]

Measures: Follow-up interview

- Chronic pain at three months after surgery was defined using two methods:
  - Method 1, denoting any pain: On 11-point numerical scales ranging from 0 to 10, any non-zero rating of either current pain or worst, least, or average pain within the past week
  - Method 2, denoting moderate-to-severe pain: On a 0 to 10 numerical rating scale, a rating greater than 4 for worst pain within the last week. This method was based on the results of a recent study indicating that worst pain ratings 1-4 correspond with mild pain, 5-6 with moderate pain, and 7-10 with severe pain[7]
- 54 participants have been interviewed for the three-month follow-up as of May 1, 2000.
- Based on Method 1, 29 participants had some degree of pain three months after surgery, 25 did not.
- Based on Method 2, 9 participants had moderate-to-severe pain three months after surgery, 45 did not.

Results

- One-tailed t-tests and chi-square tests comparing participants who did and did not develop chronic pain with respect to each of the measures from the initial assessment were used to test predictions based on previous prospective studies of the development of chronic pain syndromes[8].
- As can be seen from Table 1, participants who underwent either lumpectomy with axillary node dissection or mastectomy—as compared with lumpectomy without node dissection—were significantly more likely to have developed some degree of chronic pain. Similarly, those diagnosed with cancer were also more likely to report chronic pain three months after surgery.

Table 1: Demographic and Clinical Variables in Patients Reporting Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=25)	Pts. with any chronic pain (n=29)	Pts. with no/mild chronic pain (n=45)	Pts. with mod/sev chronic pain (n=9)
Age (years)	59.0	54.9†	56.9	56.3
Malignancy (% pts.)	62.5	82.8†	70.5	88.9
Type of surgery (%)				
Lumpectomy (n=26)	64.0	34.5*	53.3	22.2†
Lumpectomy w/nodes or mastectomy (n=28)	36.0	65.5	46.7	77.8
Biopsy taken (%)	56.0	67.9	59.1	77.8
Pre-op health (1-6)	2.4	2.1	2.2	2.2

Note. Statistical significance levels in the second and fourth columns reflect the results of two-tailed t-tests and chi-square tests:
† $p < .10$; * $p < .05$

- As can be seen from Table 2, participants who developed chronic pain reported greater pre-operative pain and early post-operative pain (within 48 hours after surgery) than participants who did not. Composite ratings refer to averages of current, least, worst, and average pain for the week prior to the pre-operative assessment and over the 24 hours prior to the early post-operative assessment.

Table 2: Pre-operative (week prior to surgery) and Early Post-operative (24 hours after surgery) Pain Ratings (0-10) in Patients Reporting Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=25)	Pts. with any chronic pain (n=29)	Pts. with no/mild chronic pain (n=45)	Pts. with mod/sev chronic pain (n=9)
Pre-op average	0.2	0.8*	0.4	1.1†
Pre-op composite	0.3	0.8†	0.4	1.1†
Post-op 24-hr. average	2.8	2.1	2.6	3.3
Post-op composite	2.6	2.7	2.4	3.7*

Note. Statistical significance levels in the second and fourth columns reflect the results of one-tailed t-tests and chi-square tests:
† $p < .10$; * $p < .05$; ** $p < .01$

- As can be seen from Table 3, participants who developed any degree of chronic pain (according to Method 1) or moderate-to-severe chronic pain (using Method 2) had greater pre-operative anxiety than did those who did not develop chronic pain.

- Although the differences between groups were not significant for either measure of depression, patients who developed pain at three months showed a nonsignificant trend toward greater depression than those who did not.

Table 3: Psychological Distress in Patients Reporting Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=25)	Pts. with any chronic pain (n=29)	Pts. with no/mild chronic pain (n=45)	Pts. with mod/sev chronic pain (n=9)
HAM-D	4.0	4.9	4.2	6.4
BDI	3.8	5.3	4.3	6.3
HAM-A	4.1	4.9	4.1	6.8†
STAI	33.5	38.2†	34.6	43.2*

Note. Statistical significance levels in the second and fourth columns reflect the results of one-tailed t-tests and chi-square tests:
† $p < .10$; * $p < .05$

- As can be seen from Table 4, participants who developed any (according to Method 1) or moderate-to-severe chronic pain (using Method 2) had greater disease conviction than participants who did not develop chronic pain.

Table 4: Illness Concern in Patients Who Developed Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=25)	Pts. with any chronic pain (n=29)	Pts. with no/mild chronic pain (n=45)	Pts. with mod/sev chronic pain (n=9)
IBQ	3.4	5.1†	4.0	6.2†
SAS	22.4	23.3	23.2	21.2

Note. Statistical significance levels in the second and fourth columns reflect the results of one-tailed t-tests:
† $p < .10$

Conclusions & Implications

- Type of surgery, malignancy, pre-operative pain, early post-operative acute pain, higher pre-operative state anxiety, and greater illness concern were found to be risk factors for the development of chronic pain following surgical procedures for breast cancer.
- Additional risk factors may be identified when the sample is fully enrolled (n=200).
- Identification of risk factors for chronic pain syndromes following breast surgery will enhance understanding of the processes by which they develop and may lead to the development of more effective preventive interventions and treatment approaches.

References

1. Maunsell, E., Brisson, J., Deschenes, L. (1993). Arm problems and psychological distress after surgery for breast cancer. *Canadian Journal of Surgery*, 36:315-320.
2. Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry,* 23:56-62.
3. Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry,* 4:561-571.
4. Spielberger, C.D. (1977). *State-trait anxiety inventory.* Palo Alto: Consulting Psychologists Press.
5. Pilowsky, I. (1989). Pain and illness behaviour: Assessment and management. In P.D. Wall, R. Melzack (Eds.), *Advances in pain research and therapy, vol. 5: Proceedings of the Third World Congress on Pain.* New York: Raven.
6. Barsky, A.J., Wyshak, G., Klerman, G.L. (1990). The somatosensory amplification scale and its relationship to hypochondriasis. *Journal of Psychiatric Research,* 24:323-334.
7. Serlin, R.C., Mendoza, T.R., Nakamura, Y., Edwards, K.R., Cleeland, C.S. (1995). When is cancer pain mild, moderate, or severe? Grading pain severity by its interference with function. *Pain,* 61:277-284.
8. Dworkin, R.H. (1997). Which individuals with acute pain are most likely to develop a chronic pain syndrome? *Pain Forum,* 6:127-136.

Acknowledgement

The U.S. Army Medical Research and Materiel Command under DAMD17-98-1-8238 supported this work.

Chronic Pain Following Breast Cancer Surgery: Prevalence and Risk Factors

Dale I. Kulick, Laura A. Hogan, Elna M. Nagasako, Carl H. Andrus and Robert H. Dworkin

University of Rochester Medical Center, Rochester, New York

Introduction

As many as 55% of women who undergo surgery for breast cancer develop post-surgical pain that may persist for months to years[1]. Although little is known about such pain syndromes once they have become chronic (i.e., at least three months following surgery), it is clear that patients can be significantly disabled and may experience substantial reductions in quality of life. The primary aims of this study are to identify risk factors for chronic pain following surgery for breast cancer, characterize its natural history, and examine its impact on women's quality of life.

Methods

Subjects

- 87 patients who have undergone breast surgery for cancer (150 anticipated by conclusion of study).
- English-speaking and at least 18 years of age.
- Recruited from surgical service at Strong Memorial Hospital, Rochester, NY.

Procedures

- Women scheduled for breast surgery for cancer who authorized the release of their names and telephone numbers to the study coordinator were contacted to describe the nature of the study and determine interest in participation.
- Those who agreed to participate were interviewed pre-operatively, within two weeks of surgery.
- A variety of interview and questionnaire measures of demographic, medical, pain, and psychosocial status were administered at this initial assessment.
- Post-operative pain and analgesic use were assessed via telephone interviews at 2 and 10 days after surgery.
- At 1, 3, 7, and 12 months following surgery, telephone interviews were conducted in which persisting surgery-related pain and disability, analgesic use, interim health status and treatment history, and psychological distress were assessed.
- The individuals conducting these follow-up interviews were blind with respect to the information collected during the initial assessment.

Measures: Initial assessment

- The present analyses are focused on comparing patients who did and did not report some degree of persisting pain at three months after surgery with respect to measures administered at the initial assessment.
- Age, presence of pre-operative breast pain, presence of malignancy, history of diagnostic core biopsy, type of surgery, acute post-operative pain (within 48 hours of surgery), self-reported overall pre-operative health, and four sets of psychosocial measures hypothesized to predict chronic pain were examined:

1. Depression: Hamilton Rating Scales - Depression (HAM-D)[2] and Beck Depression Inventory (BDI)[3]
2. Anxiety: Hamilton Rating Scales - Anxiety (HAM-A)[4] and State-Trait Anxiety Inventory, state version (STAI)[5]
3. Disease conviction: Illness Behavior Questionnaire disease conviction scale (IBQ)[6]
4. Somatosensory focus: Somatosensory Amplification Scale (SAS)[7]

Measures: Follow-up interview

- Chronic pain at three months after surgery was defined using two methods:
  - Method 1, denoting any pain: On 11-point numerical scales ranging from 0 to 10, any non-zero rating of either current pain or worst, least, or average pain within the past week.
  - Method 2, denoting moderate-to-severe pain: On a 0 to 10 numerical rating scale, a rating greater than 4 for worst pain within the last week. This method was based on the results of a recent study indicating that worst pain ratings 1-4 correspond with mild pain, 5-6 with moderate pain, and 7-10 with severe pain[8].
- 87 participants have been interviewed for the three-month follow-up as of April 1, 2001.

Results

- Two-tailed t-tests and chi-square tests comparing participants who did and did not develop chronic pain with respect to each of the measures from the initial assessment were used to test predictions based on previous prospective studies of the development of chronic pain syndromes[9].
- Based on Method 1, 43 (49%) participants reported some degree of pain three months after surgery, 44 (51%) did not.
- Based on Method 2, 13 (15%) participants reported moderate-to-severe pain three months after surgery, 74 (85%) did not.
- As can be seen from Table 1, participants who were younger as well as those who were diagnosed with cancer were significantly more likely to have developed some degree of chronic pain by three months after surgery.

Table 1: Demographic and Clinical Variables in Patients Reporting Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=44)	Pts. with any chronic pain (n=43)	Pts. with no/mild chronic pain (n=74)	Pts. with mod/sev chronic pain (n=13)
Age (years)	60.1	55.1*	58.0	55.7
Malignancy (% pts.)	60.5	80.5*	66.2	92.3†
Type of surgery (%)				
Lumpectomy (n=44)	59.1	40.9	90.9	30.8
Lumpectomy w/nodes or mastectomy (n=43)	41.9	58.1	79.1	69.2
Biopsy taken (%)	65.9	69.8	66.2	76.9
Pre-op health (1-6)	2.2	2.2	2.1	2.4

Note. Statistical significance levels in the second and fourth columns reflect the results of two-tailed t-tests and chi-square tests:
† $p \leq .10$; * $p \leq .05$

- As can be seen from Table 2, participants who developed chronic pain reported greater pre-operative pain and early post-operative pain than participants who did not. Composite ratings refer to averages of current, least, worst, and average pain for the week prior to the pre-operative assessment and over the 24 hours prior to the early post-operative assessment.

Table 2: Pre-operative (week prior to surgery) and Early Post-operative (24 hours after surgery) Pain Ratings (0-10) in Patients Reporting Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=44)	Pts. with any chronic pain (n=43)	Pts. with no/mild chronic pain (n=74)	Pts. with mod/sev chronic pain (n=13)
Pre-op average	0.1	0.7*	0.3	0.8
Pre-op composite	0.2	0.7*	0.4	0.7
Post-op 24-hr. average	2.6	3.2	2.6	4.2*
Post-op composite	2.4	3.1†	2.5	4.1*

Note. Statistical significance levels in the second and fourth columns reflect the results of two-tailed t-tests and chi-square tests:
† $p \leq .10$; * $p \leq .05$

- As can be seen from Table 3, participants who developed moderate-to-severe chronic pain (according to Method 2) had greater pre-operative anxiety than those who did not develop chronic pain.
- Although the differences between groups were not significant for either measure of depression, patients who developed pain at three months (according to Method 1) showed a nonsignificant trend toward greater pre-operative depression than those who did not.

Table 3: Psychological Distress in Patients Reporting Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=44)	Pts. with any chronic pain (n=43)	Pts. with no/mild chronic pain (n=74)	Pts. with mod/sev chronic pain (n=13)
HAM-D	4.6	5.9	4.9	7.7
BDI	4.5	6.6†	5.1	7.9
HAM-A	4.5	5.8	4.7	7.9*
STAI	35.0	36.7	34.9	41.2†

Note. Statistical significance levels in the second and fourth columns reflect the results of two-tailed t-tests and chi-square tests:
† $p \leq .10$; * $p \leq .05$

- As can be seen from Table 4, participants who developed moderate-to-severe chronic pain (using Method 2) had greater disease conviction than participants who did not develop chronic pain. Additionally, participants who developed any chronic pain (according to Method 1) demonstrated significantly greater pre-operative somatosensory focus than those who did not report chronic pain.

Table 4: Illness Concern in Patients Who Developed Various Levels of Chronic Pain Three Months After Breast Surgery

Measure	Pts. with no chronic pain (n=44)	Pts. with any chronic pain (n=43)	Pts. with no/mild chronic pain (n=74)	Pts. with mod/sev chronic pain (n=13)
IBQ	3.6	4.7	3.9	5.5†
SAS	21.7	24.5*	23.0	23.3

Note. Statistical significance levels in the second and fourth columns reflect the results of two-tailed t-tests:
† $p \leq .10$; * $p \leq .05$

- To further examine the relationships among the risk factors for the development of chronic pain, a logistic regression analysis was conducted in which age and presence of malignancy were entered first in the model, the two pre-operative and two acute post-operative pain ratings were entered second in stepwise fashion, and the independent contributions of psychosocial risk factors were examined last. As proposed by Hosmer and Lemeshow (1989)[10], measures were included in these analyses when their univariate tests had p values of $< .25$.
- Results of these analyses revealed that age and presence of malignancy both contributed significantly to the prediction of chronic pain at three months post-surgery, and that the fit of the model was significantly improved when the rating of average pre-operative pain over the week prior to the initial assessment (log-likelihood $\chi^2 = 6.24$, $df = 1$, $p = .01$) was entered in the analysis. Subsequent entry of psychological distress and illness concern measures did not significantly improve the fit of the model.

Conclusions and Implications

- Age, malignancy, pre-operative pain, early post-operative acute pain, higher pre-operative anxiety, and greater illness concern were found to be risk factors for the development of chronic pain following surgical procedures for breast cancer in the univariate analyses.
- Identification of risk factors for chronic pain syndromes following breast cancer surgery will enhance understanding of the processes by which they develop and may lead to the development of more effective preventive interventions and treatment approaches.

References

1. Maunsell, E., Brisson, J., Deschenes, L. (1992). Arm problems and psychological distress after surgery for breast cancer. *Canadian Journal of Surgery*, 36:315-320.
2. Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*, 23:56-62.
3. Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, 4:561-571.
4. Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology*, 32:50-55.
5. Spielberger, C.D. (1977). *State-trait anxiety inventory*. Palo Alto: Consulting Psychologists Press.
6. Pilowsky, I. (1995). Pain and illness behaviour: Assessment and management. In P.D. Wall, R. Melzack (Eds.), *Advances in pain research and therapy, vol. 2: Proceedings of the Third World Congress on Pain*. New York: Raven.
7. Barsky, A.J., Wyshak, G., Klerman, G.L. (1990). The somatosensory amplification scale and its relationship to hypochondriasis. *Journal of Psychiatric Research*, 24:323-334.
8. Serlin, R.C., Mendoza, T.R., Nakamura, Y., Edwards, K.R., Cleeland, C.S. (1995). When is cancer pain mild, moderate, or severe? Grading pain severity by its interference with function. *Pain*, 61:277-284.
9. Dworkin, R.H. (1997). Which individuals with acute pain are most likely to develop a chronic pain syndrome? *Pain Forum*, 6:127-136.
10. Hosmer, D.W., Jr., Lemeshow, S. (1989). *Applied logistic regression*. New York: Wiley.

Acknowledgment

The U.S. Army Medical Research and Materiel Command under DAMD17-98-1-8238 supported this work by a grant to the fifth author.